What is claimed is:

1. An *in vitro* method of making sequence variants from at least one heteroduplex polynucleotide where said heteroduplex has at least two non-complementary nucleotide base pairs, said method comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein one or more variants are made.

2. An *in vitro* method of making sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs, said method comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity; and

c. allowing sufficient time for the percentage of complementarity to increase,

wherein at least one or more variants are made.

3. The method of claim 2 wherein said heteroduplex polynucleotide is circular.

4. The method of claim 2 wherein said heteroduplex polynucleotide is linear.

5. The method of claim 3 or 4 wherein said heteroduplex polynucleotide is a replicon.

6. The method of claim 2 wherein said variants have different amounts of complementarity.

7. The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, and strand cleavage activity are added sequentially.

8. The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, and strand cleavage activity are added concurrently.

9. The method of claim 2 in step (b) further comprising ligase activity.

10. The method of claim 2 further comprising a step of,

(d) adding a ligase.

11. The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, ligase activity, and strand cleavage activity are added sequentially.

12. The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, ligase activity, and strand cleavage activity are added concurrently.

13. The method of claim 9 wherein said ligase is T4 DNA ligase, E. coli DNA ligase, or Taq DNA ligase.

14. The method of claim 2 wherein said agent with strand cleavage activity is an enzyme.

15. The method of claim 2 wherein said agent with strand cleavage activity is a mismatch endonuclease.

16. The method of claim 2 wherein said agent with strand cleavage activity is selected from the group consisting of CEL I, T4 endonuclease VII, T7 endonuclease I, S1 nuclease, BAL-31 nuclease, FEN1, cleavase, pancreatic DNase I, SP nuclease, mung bean nuclease, and nuclease P1.

17. The method of claim 2 wherein said agent with strand cleavage activity is a chemical.

18. The method of claim 2 wherein said agent with strand cleavage activity is selected from the group consisting of potassium permanganate, tetraethylammonium acetate, sterically bulky photoactivatable DNA intercalators, [Rh(bpy)2(chrysi)]3+, osmium tetroxide with piperidine, and hydroxylamine with piperidine.

19. The method of claim 2 wherein said agent with strand cleavage activity is ionizing radiation, or kinetic radiation.

20. The method of claim 2 wherein said agent with polymerase activity is T4 DNA polymerase.

21. The method of claim 2 wherein said agent with polymerase activity is T7 DNA polymerase.

22. The method of claim 2 wherein said agent with both polymerase activity and 3′ to 5′ exonuclease activity is T4 DNA polymerase, T7 DNA polymerase, E. coli Pol 1, or Pfu DNA polymerase.

23. The method of claim 2 wherein said agent with both polymerase activity and 5′ to 3′ exonuclease activity is E. coli Pol 1.

24. The method of claim 2 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase.

25. The method of claim 2 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase.

26. The method of claim 2 wherein an effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase.

27. An in vitro method of increasing diversity in a population of sequences, comprising: preparing at least one heteroduplex polynucleotide; combining said heteroduplex polynucleotide with an effective amount of an agent or agents with 3′ to 5′ exonuclease activity, polymerase activity and strand cleavage activity; and allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

28. The method of claim 27 wherein said heteroduplex polynucleotide is circular.

29. The method of claim 27 wherein said heteroduplex polynucleotide is linear.

30. The method of claim 3 or 4 wherein said heteroduplex polynucleotide is a replicon.

31. The method of claim 27 wherein said variants have different amounts of complementarity.

32. The method of claim 27 wherein said enzymes having 3′ to 5′ exonuclease activity, polymerase activity, and strand cleavage activity are added sequentially.

33. The method of claim 27 wherein said enzymes having 3′ to 5′ exonuclease activity, polymerase activity, and strand cleavage activity are added at the same time.

34. The method of claim 27 further comprising adding a ligase.

35. The method of claim 9 wherein said ligase is T4 DNA ligase, E. coli DNA ligase, or Taq DNA ligase.

36. The method of claim 27 wherein said agent with strand cleavage activity is an enzyme.

37. The method of claim 27 wherein said agent with strand cleavage activity is a mismatch endonuclease.

38. The method of claim 27 wherein said agent with strand cleavage activity is selected from the group consisting of CEL I, T4 endonuclease VII, T7 endonuclease I, S1 nuclease, BAL-31 nuclease, FEN1, cleavase, pancreatic DNase I, SP nuclease, mung bean nuclease, nuclease P1.

39. The method of claim 27 wherein said agent with strand cleavage activity is a chemical.

40. The method of claim 27 wherein said agent with strand cleavage activity is selected from the group consisting of potassium permanganate, tetraethylammonium acetate, sterically bulky photoactivatable DNA intercalators, [Rh(bpy)2(chrysi)]3+, osmium tetroxide with piperidine, and hydroxylamine with piperidine.

41. The method of claim 27 wherein said agent with strand cleavage activity is ionizing radiation, or kinetic radiation.

42. The method of claim 27 wherein said agent with polymerase activity is T4 DNA polymerase.

43. The method of claim 27 wherein said agent with polymerase activity is T7 DNA polymerase.

44. The method of claim 27 wherein said agent with both polymerase activity and 3′ to 5′ exonuclease activity is T4 DNA polymerase, T7 DNA polymerase, E. coli Pol 1, or Pfu DNA polymerase.

45. The method of claim 27 wherein said agent with both polymerase activity and 5′ to 3′ exonuclease activity is E. coli Pol 1.

46. The method of claim 27 wherein said effective amount of strand cleavage activity, exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase respectively.

47. The method of claim 27 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase respectively.

48. The method of claim 27 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase respectively.

49. The method of claim 27 wherein an effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase respectively.

50. An in vitro method of increasing diversity in a population of sequences, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

51. A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity, and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide

to increase, wherein diversity in the population is increased; and

d. screening or selecting a population of variants for the desired functional property.

52. A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity, and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide to increase, wherein diversity in the population is increased;

d. converting DNA to RNA; and

e. screening or selecting a population of ribonucleic acid variants for the desired functional property.

53. A method of obtaining a polypeptide having a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or

agents with exonuclease activity, polymerase activity and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of said heteroduplex polynucleotide to increase,

d. converting said heteroduplex polynucleotide to RNA, and said RNA to a polypeptide; and

e. and screening or selecting a population of polypeptide variants for said desired functional property.

54. A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of said heteroduplex polynucleotide to increase,

d. screening or selecting for a population of variants having a desired functional property;

e. denaturing said population of variants to obtain single strand polynucleotides;

f. annealing said single strand polynucleotides to form at least one second heteroduplex polynucleotide;

g. combining said second heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity; and

h. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide to increase.

55. The method of claim 54 wherein said heteroduplex polynucleotide is greater than 95% identical.

56. The method of claim 54 wherein said heteroduplex polynucleotide is about 95% identical.

57. The method of claim 54 wherein said heteroduplex polynucleotide is about 90% identical.

58. The method of claim 54 wherein said heteroduplex polynucleotide is about 85% identical.

59. The method of claim 54 wherein said heteroduplex polynucleotide is about 80% identical.

60. The method of claim 54 wherein said heteroduplex polynucleotide is about 75% identical.

61. The method of claim 2 wherein the heteroduplex polynucleotide is about 1000Kb.

62. The method of claim 2 wherein the heteroduplex polynucleotide is about 10,000Kb.

63. The method of claim 2 wherein the heteroduplex polynucleotide is about 100,000Kb.

64. A kit used for increasing diversity in a population of sequences, comprising: preparing at least one heteroduplex polynucleotide; combining said heteroduplex polynucleotide with an effective amount of an agent or agents with 3' to 5' exonuclease activity, polymerase activity and strand cleavage activity; and allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

65. The kit of claim 64 further comprising having a ligase activity.